

**REMARKS**

Applicants thank the Examiner for the very thorough consideration given the present application. Claims 2-12, 15 and 16 are currently pending in this application. No new matter has been added by way of the present amendment. The amendments to claims 2, 5, 6, 7 and 9 are merely editorial and non-narrowing in nature. Accordingly, no new matter has been added.

In view of the amendments and remarks herein, Applicants respectfully request that the Examiner withdraw all outstanding rejections and allow the currently pending claims.

**Claim Objections**

Claims 2, 5, 6, 7 and 9 are objected to. Applicants respectfully traverse.

Claims 2, 5, 6, 7 and 9 have been amended to address the issues identified by the Examiner. Accordingly, this objection is moot.

Reconsideration and withdrawal of this objection are respectfully requested.

**Issues Under 35 U.S.C. § 103**

Claims 2-12, 15 and 16 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,811,446 (hereinafter “Thomas”), in view of U.S. Patent 5,994,372 (hereinafter “Yaksh”), and U.S. Patent 5,116,868 (hereinafter “Chen”). Applicants respectfully traverse.

The Examiner asserts that Thomas discloses the treatment of a variety of disorders of the eye by topical administration of a solution containing a therapeutically effective amount of histidine to reduce ocular inflammation. The Examiner acknowledges that Thomas fails to teach

or suggest the administration of beta-hydroxybutyric acid or salts thereof in the treatment of eye diseases, and relies on the teachings of Yaksh and Chen to cure the deficiencies of Thomas.

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, the Examiner must make the factual determinations set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). “[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability.” *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992). A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *KSR Int’l Co. v Teleflex Inc.*, 82 USPQ 2d 1385 (U.S. 2007). There must be a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. *Id.* The Supreme Court of the United States has recently held that the “teaching, suggestion, motivation test” is a valid test for obviousness, albeit one which cannot be too rigidly applied. *Id.* “[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *Id.* (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

Thomas teaches the treatment of allergic conjunctivitis and blepharitis with a histidine based solution. Thomas teaches that the histidine formulation can include alpha- or beta-hydroxybutyric acids, which are useful in cosmetic materials to “promote cell regeneration activity.” However, Applicants submit that the “cell regeneration activity” mentioned in Thomas bears no relation to the presently claimed method for treating tear abnormalities.

Thomas' invention targets diseases such as glaucoma and age-related macular degeneration, which are diseases of tissues whose cells cannot be regenerated by cell division, such as the retinal tissue and the optical nerve, found in the posterior chamber of the eye. In contrast, the present invention targets cells (tissues) that can be regenerated by cell division, such as the corneal epithelial cells. Thus, Applicants submit that cell regeneration activity would not be useful in the treatment of the diseases as listed in present claim 12. Yaksh and Chen fail to cure the deficiencies of Thomas.

Yaksh discloses a drug for treating hyperalgesia in the peripheral nervous system. The nerve terminals not only accept pain, but also secrete a chemical substance known as "substance P" by axon reflex. This chemical substance acts on a mast cell to release histamine, produces another algestic substance and causes vascular dilation. When a tissue is damaged, various algestic substances, such as prostaglandin, potassium and bradykinin, are secreted. In this state where the nerve terminal is continuously immersed in algestic substances, sensitivity to pain of a nerve significantly rises, thereby developing (peripheral) hyperalgesia. However, Applicants submit that the mechanism by which (peripheral) hyperalgesia develops involves algestic substances, which differs completely from the mechanisms involved in dry eye, which are targeted by the present invention. As such, the skilled artisan, wanting to treat the diseases described in present claim 12, would not look to an anti-hyperalgesia compound, such as that described by Yaksh.

Chen discloses an ophthalmic irrigation solution containing  $\beta$ -hydroxybutyric acid. However, Chen does not teach or suggest the use of the solution as a treating drug (see, e.g., col.

6, lines 7-8, wherein it is explicitly disclosed that the ophthalmic irrigation solution is not intended for use as a therapeutic agent).

Ophthalmic irrigation solutions are used to clean the inside of the eye and to prevent drying on the surface of the eye during ophthalmic surgery. As such, one skilled in the art would not think of using the ophthalmic irrigation solution of Chen for the treatment of the eye diseases listed in claim 12 of the present application.

Evidently, the cited references, alone or in combination, fail to teach or suggest every limitation of the instant invention. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

### **Conclusion**

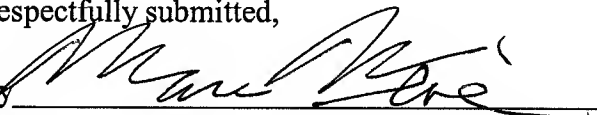
All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and objections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Vanessa Perez-Ramos, Reg. No. 61,158, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: October 27, 2009

Respectfully submitted,

By 

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